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Supplement to form 1449APTO

# INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet 1 of 4

Complete if Known

Application Number 10/091,759  
Filing Date March 5, 2002  
First Named Inventor Adnan M.M. Mjalli  
Group Art Unit 1614  
Examiner Name Unassigned  
Attorney Docket Number 41305-271123 (2002)  
Express Mail Certificate EV 032 196 842 US

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## U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No. <sup>1</sup>	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication Cited Document MM-DD-YYYY	Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear
		Number	Kind Code <sup>2</sup> (if known)			
Pro	1	4,166,452		Generales, Jr.	09-04-79	
	2	4,265,874		Bonsen, et al.	05-05-81	
	3	4,356,108		Schwab, et al.	10-26-82	
	4	4,873,313		Crawford, et al.	10-10-89	
	5	5,202,424		Vlassara, et al.	04-13-93	
	6	5,585,344		Vlassara, et al.	12-17-96	
	7	5,688,653		Ulrich, et al.	11-18-97	
	8	5,864,018		Morser, et al.	01-26-99	
	9	5,939,526		Gaugler, et al.	08-17-99	
	10	6,100,098		Newkirk	08-08-00	

## FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No. <sup>1</sup>	Foreign Patent Document			Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T <sup>3</sup>
		Office <sup>5</sup>	Number <sup>4</sup>	Kind Code <sup>2</sup> (if known)				
Pro	11	WO	00/20458		The Trustees of Columbia University in NYC	04-13-00		✓
	12	WO	00/20621		The Trustees of Columbia University in NYC	04-13-00		✓
	13	WO	97/26913		The Trustees of Columbia University in NYC	07-31-97		✓
	14	WO	97/39121		Schering Aktiengesellschaft	10-23-97		✓
	15	WO	97/39125		Schering Aktiengesellschaft	10-23-97		✓
	16	WO	98/22138		The Trustees of Columbia University in NYC	05-28-98		✓
	17	WO	99/07402		The Trustees of Columbia University in NYC	02-18-99		✓
	18	WO	99/18987		The Trustees of Columbia University in NYC	04-22-99		✓
	19	WO	99/54485		The Trustees of Columbia University in NYC	10-28-99		✓
	20	WO	95/09838		Merrell Dow Pharmaceuticals Inc.	04-13-95		✓
Pro	21	WO	95/35279		Merrell Pharmaceuticals Inc.	12-28-95		✓
	22	WO	97/22618		Vertex Pharma- ceuticals Incorporated	06-26-97		✓
	23	WO	96/32385		Hoechst Marion Roussel Inc.	10-17-96		✓
	24	WO	99/50230		Vertex Pharma- ceuticals Incorporated	10-07-99		✓

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		Group Art Unit	1614
		Examiner Name	Unassigned
		Attorney Docket Number	41305-271123 (2002)
Express Mail Certificate	EV 032 196 842 US	TECH CENTER 1600/2900	

No ↑ ↓	25	GB	2 005 674		Carlo Erba S.p.A.	04-25-79		✓
	26	WO	98/33492		Fox Chase Cancer Center	08-06-98		✓
	27	WO	99/25690		University of Kansas Medical Center	05-27-99		✓
Mo ↓	28	WO	01/12598		The Trustees of Columbia University in New York City, NY	02-22-01		✓

OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS			
Examiner Initials	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>2</sup>
No	29	Albercio, F. & Carpino, L.A., "Coupling Reagents and Activation" <i>Methods in Enzymology</i> 289:104-126, Academic Press, San Diego (1997)	✓
	30	Barton, J.W., "In Protection of N-H Bonds and NR <sub>3</sub> " <i>Protective Groups in Organic Chemistry</i> , J.F.W. McOmie, ED., Plenum Press, New York, NY (1973)	✓
	31	Berge, S.M., et al., "Pharmaceutical Salts" <i>Journal of Pharmaceutical Sciences</i> 66:1-19 (1977)	✓
	32	Chitaley, K., et al., "Antagonism of Rho-Kinase Stimulates Rate Penile Erection via a Nitric Oxide-Independent Pathway" <i>Nature Medicine</i> 7:119-122 (2002)	✓
	33	Degenhardt, T.P., et al., "Chemical Modification of Proteins by Methylglyoxal" <i>Cell Mol. Biol.</i> , 44:1139-1145 (1998)	✓
	34	Dyer, D.G., et al., "Accumulation of Maillard Reaction Products in Skin Collagen in Diabetes and Aging" <i>J. Clin. Invest.</i> , 91:2463-2469 (1993)	✓
	35	Dyer, D.G., et al., "Formation of Pentosidine during Nonenzymatic Browning of Proteins by Glucose" <i>J. Biol. Chem.</i> , 266:11654-11660 (1991)	✓
	36	Greene, T.W., "Protection for the Amino Group" <i>Protective Groups in Organic Synthesis</i> , John Wiley and Sons, New York, NY, Chapter 7 (1981)	✓
	37	Hammes, H.P., et al., "Diabetic Retinopathy Risk Correlates with Intracellular Concentrations of the Glycoxidation Product N <sup>ε</sup> -(Carboxymethyl) Lysine Independently of Glycohaemoglobin Concentrations" <i>Diabetologia</i> , 42:603-607 (1999)	✓
	38	Hoffman, M.A., et al., "RAGE Mediates a Novel Proinflammatory Axis: A Central Cell Surface Receptor for S100/Calgranulin Polypeptides" <i>Cell</i> , 97:889-901 (1999)	✓
No	39	Hori, O., et al., "The Receptor for Advanced Glycation End Products (RAGE) Is a Cellular Binding site for Amphoterin" <i>J. Biol. Chem.</i> , 270:25752-761 (1995)	✓
	40	Huttunen, H.J., et al., "Receptor for Advanced Glycation End Products (RAGE)-Mediated Neurite Outgrowth and Activation of NF-Kappa B Require the Cytoplasmic Domain of the Receptor But Different Downstream Signaling Pathways" <i>J. Biol. Chem.</i> 274(28):19919-24 (1999)	✓

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First Named Inventor Adnan M.M. Mjalli  
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Examiner Name Unassigned  
Attorney Docket Number 41305-271123 (2001-  
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41	Kumar, S.R., et al., "RAGE at the Blood-Brain Barrier Mediates Neurovascular Dysfunction Caused by Amyloid $\beta_{1-40}$ Peptide" <i>Neurosci. Program</i> , 141-#255.19 (2000)	✓
42	Leder, A. et al., "v-HA-ras Transgene Abrogates the Initiation Step in Mouse Skin Tumorigenesis: Effects of Phorbol Esters and Retinoic Acid" <i>Proc. Natl. Acad. Sci., USA</i> , 87:9178-9182 (1990)	✓
43	Li, J. et al., "Sp1-Binding elements in the Promoter of RAG Are Essential for Amphoterin-Mediated Gene Expression in Cultured Neuroblastoma Cells." <i>J. Biol. Chem.</i> , 273:30870-30878 (1998)	✓
44	Li, J. et al., "Characterization and Functional Analysis of the Promoter of RAGE, the Receptor for Advanced Glycation End Products," <i>J. Biol. Chem.</i> , 272:16498-16506 (1997)	✓
45	Lugering, N. et al., "The Myeloic Related Protein MRP8/14 (27E10 Antigen)—Usefulness as a Potential Marker for Disease Activity in Ulcerative Colitis and Putative Biological Function" <i>Eur. J. Clin. Invest.</i> , 25:659-664 (1995)	✓
46	Miyata, T. et al., " $\beta_2$ -Microglobulin Modified with Advanced Glycation End Products Is a Major Component of Hemodialysis-Associated Amyloidosis" <i>J. Clin. Invest.</i> , 92:1243-1252 (1993)	✓
47	Miyata, T. et al., "The Receptor for Advanced Glycation End Products (RAGE) Is a Central Mediator of the Interaction of AGE- $\beta_2$ Microglobulin with Human Mononuclear Phagocytes Via an Oxidant-Sensitive Pathway" <i>J. Clin. Invest.</i> , 98:1088-1094 (1996)	✓
48	Neeper, M., et al., "Cloning and Expression of a Cell Surface Receptor for Advanced Glycosylation End Products of Proteins" <i>J. Biol. Chem.</i> , 267:14998-15004 (1992)	✓
49	Parkkinen, J. et al., "Amphoterin, the 30-kDa Protein in a Family of HMG1-Type Polypeptides" <i>J. Biol. Chem.</i> , 268:19726-19738 (1993)	✓
50	Rammes, A. et al., "Myeloid-Related Protein (MRP) 8 and MRP 14, Calcium-Binding Proteins of the S100 Family, Are Secreted by Activated Monocytes via a Novel, Tubulin-Dependent Pathway" <i>J. Biol. Chem.</i> , 272:9496-9502 (1997)	✓
51	Rauvala, H. et al., "Isolation and Some Characteristics of an Adhesive Factor of Brain That Enhances Neurite Outgrowth in Central Neurons" <i>J. Biol. Chem.</i> , 262:16625-16635 (1987)	✓
52	Reddy, S. et al., "N <sup>ε</sup> -(Carboxymethyl) Lysine Is a Dominant Advanced Glycation End Product (AGE) Antigen in Tissue Proteins" <i>Biochem.</i> , 34:10872-10878 (1995)	✓
53	Schafer, B.W., et al., "The S100 Family of EF-Hand Calcium-Binding Proteins: Functions and Pathology" <i>TIBS</i> , 21:134-140 (1996)	✓
54	Schleicher, E.D., et al., "Increased Accumulation of the Glycoxidation Product N <sup>ε</sup> -(Carboxymethyl) Lysine in Human Tissues in Diabetes and Aging" <i>J. Clin. Invest.</i> , 99(3):457-468 (1997)	✓
55	Schmidt, A.M. et al., "The Dark Side of Glucose" <i>Nature Med.</i> , 1:1002-1004 (1995)	✓

March 2002

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**INFORMATION DISCLOSURE STATEMENT BY APPLICANT**

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Sheet 4 of 4

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Application Number	10/091,759
Filing Date	March 5, 2002
First Named Inventor	Adnan M.M. Mjalli
Group Art Unit	1614
Examiner Name	Unassigned
Attorney Docket Number	41305-271123 (2001-21)

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Pro	56	Schmidt, A.M., et al., "The V-Domain of Receptor for Advanced Glycation Endproducts (RAGE) Mediates Binding of AGEs: A Novel Target for Therapy of Diabetic Complications." <i>Supplement to Circulation</i> Vol. 96, #194 (1997)	✓
↑	57	Taguchi, A. et al., "Blockade of RAGE—Amphoterin Signalling Suppresses Tumour Growth and Metastases" <i>Nature</i> , 405:354-360 (2000)	✓
	58	Tanaka, N., et al., "The Receptor for Advanced Glycation End Products is Induced by the Glycation Products Themselves and Tumor Necrosis Factor-α through Nuclear Factor-κB, and by 17β-Estradiol through Sp-1 in Human Vascular Endothelial Cells" <i>J. Biol. Chem.</i> , 275:25781-25790 (2000)	✓
	59	Teillet et al., "Food Restriction Prevents Advanced Glycation End Product Accumulation and Retards Kidney Aging in Lean Rats" <i>J. Am. Soc. Nephrol.</i> , 11:1488-1497 (2000)	✓
	60	Vlassara, H., "Advanced Glycation End-Products and Atherosclerosis" <i>The Finnish Medical Society DUODECIM, Ann. Med.</i> , 28:419-426 (1996)	✓
	61	Wautier et al., "Receptor-Mediated Endothelial Cell Dysfunction in Diabetic Vasculopathy: Soluble Receptor for Advanced Glycation End Products Blocks Hyperpermeability in Diabetic Rats" <i>J. Clin. Invest.</i> , 97:238-243 (1996)	✓
	62	Yan, S.-D., et al., "RAGE and Amyloid-β Peptide Neurotoxicity in Alzheimer's Disease" <i>Nature</i> 382:685-691 (1996)	✓
	63	Yan, S.-D., et al., "An Intracellular Protein That Binds Amyloid-β Peptide and Mediates Neurotoxicity in Alzheimer's Disease" <i>Nature</i> , 389:689-695, (1997)	✓
	64	Yan, S.-D. et al., "Amyloid-β Peptide—Receptor for Advanced Glycation Endproduct Interaction Elicits Neuronal Expression of Macrophage-Colony Stimulating Factor: A Proinflammatory Pathway in Alzheimer Disease" <i>Proc. Natl. Acad. Sci., USA</i> , 94:5296-5301 (1997)	✓
	65	Yan, S.-D. et al., "Receptor-Dependent Cell Stress and Amyloid Accumulation in Systemic Amyloidosis" <i>Nat. Med.</i> 6:643-651 (2000)	✓
	66	Yan, S.-D. et al., "Enhanced Cellular Oxidant Stress by the Interaction of Advanced Glycation Endproducts With Their Receptors Binding Proteins" <i>J. Biol. Chem.</i> 269:9889-9897 (1994)	✓
↓	67	Zimmer, D. et al., "The S100 Protein Family: History, Function, and Expression" <i>Brain Res. Bull.</i> 37:417-429 (1995)	✓
Pro	68	International Search Report for PCT/US 01/17251 dated 8/14/01	✓
Examiner Signature <u>ASR</u>		Date Considered <u>March 2004</u>	

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformation and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Unique citation designation number. <sup>2</sup> Applicant is to place a check mark here if English language Translation is attached.

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